

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Date: February 18, 2008

In re application of:

Kelkar et al

Serial No.: 10/629,448

Filed: July 29, 2003

Group Art Unit: 1631

Examiner: **Loria Clow**

FOR: Method and Program

## Product for Discovering

## Similar Gene Expression Profiles

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18 FEB 2008

Date of Signature

SECOND AMENDED APPEAL BRIEF IN SUPPORT OF APPEAL FROM  
THE PRIMARY EXAMINER TO THE BOARD OF APPEALS

Assistant Commissioner for Patents

Washington DC 20231

Sir:

Appellants herewith submit a Second Amended Appeal Brief in support of the appeal to the Board of Patent Appeals and Interferences from the decision dated May 16, 2007 of the Primary Examiner finally rejecting claims 1-6, 10-16 and 20.

**(I) Real Party in Interest**

The real party in interest in this appeal is International Business Machines Corporation, a New York corporation, assignee of the entire right, title and interest in the claimed invention.

## (II) Related Appeals and Interferences

No other appeals or interferences are known to the Appellants, the Appellants' legal representative, or assignee that will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

(III) Status of Claims

Claims 1-6, 10-16 and 20 are pending in this application.

Claims 7-9 and 17-19 were canceled after restriction.

The rejection of claims 1-6, 10-16 and 20 under 35 U.S.C. 101 is appealed.

The rejection of claims 1, 2, 4, 6, 12, 14, 16 and 20 under 35 U.S.C. 112 has been addressed by applicant's attorney in the amendment after final and the Examiner has found applicants' arguments to be persuasive, therefore it was believed that this issue no longer existed, however in view of the Examiners comment in the Notice of Non-Compliant Appeal Brief, these remarks are repeated below as Issue I.

When this application was filed in 2003, applicants' attorney believed that providing independent claims would facilitate prosecution because they could be allowed or rejected without requiring rewriting to incorporate independent claim limitations into dependent claims when they were found to be allowable. It is understood that currently this practice is not permitted in excess of four claims and applicants' attorney regrets any inconvenience caused thereby.

(IV) Status of Amendments

The amendment filed before final has been entered.

The amendment filed after final has not been entered.

(V) Summary of Claimed Subject Matter

References to paragraphs are made to the application as published.

1. A method for determining similarity between portions of gene expression profiles in a computer comprising the steps of:

processing a number of gene expression profiles with a similar sequences algorithm that is a time and intensity invariant correlation function to obtain a data set of gene expression profile pairs and a match fraction for each gene expression profile pair;

Page 7, Line 31-Page 8, Line 9 (Paragraph 36) and Fig. 1, # 213, 215

listing gene expression profile pairs in clusters by their match fractions; **Page 8 Lines 16-26 (paragraph 38) and Fig.2 # 223**

removing a first gene expression profile from a cluster when another cluster has another gene expression profile with a higher match fraction with the first gene expression profile, unless the another gene expression profile requires a larger number of subsequences to achieve similarity with the first gene expression profile; **Page 8 Line 27-Page 9 Line 7 (paragraph 39) and Fig. 2 #**

225

repeating the removing step until all gene expression patterns are removed.

are listed in only one cluster.

(Paragraph 39) last sentence

providing output of the listing of clusters of gene

expression profiles. Page 6 Lines 24-31 and Pa

1           2. A method for determining similarity between portions of gene  
2 expression profiles comprising the steps of:

3           processing a number of gene expression profiles with a similar  
4 sequences algorithm that is a time and intensity invariant  
5 correlation function to obtain a data set of gene expression pairs  
6 and a match fraction for each pair; **Page 7,Line 31 - Page 8,Line 9**  
7 **(Paragraph 36) and Fig. 1, # 213, 215)**

8           listing gene expression pairs in clusters by their match  
9 fractions; **Page 8 Lines 16-26 (Paragraph 38) and Fig.2 # 223**

10           removing a first gene from a first cluster when the first gene  
11 is also in a second cluster which has another gene with a higher  
12 match fraction with the first gene than any of the genes in the  
13 first cluster have with the first gene, but; **Page 8 Line 27 - Page 9**  
14 **Line 7 (Paragraph 39) and Fig. 2 # 225**

15           retaining the first gene in the first cluster and removing the  
16 first gene from the second cluster when the difference between the  
17 highest match fraction of the first gene with a gene in the first  
18 cluster and the highest match fraction of the first gene with a gene  
19 in the second cluster is less than a minimum difference threshold  
20 and the number of subsequences represented in the similar gene pair  
21 having the highest match fraction in the first cluster is higher  
22 than the number of subsequences represented in the similar gene pair  
23 having the highest match fraction in the second cluster; **Page 9 Line**  
24 **18 - Page 10 Line 10 (Paragraphs 41, 42, 43 and 56) and Fig. 2 # 225**

25           repeating the removing step until all genes are listed in only  
26 one cluster; **Page 8 Line 27 - Page 9 Line 7 (Paragraph 39) last**  
27 **sentence**

28           providing output of the listing of clusters of gene  
29 expression profiles. **Page 6 Lines 24 - 31 and Page 7 Lines 19-24**  
30 **(Paragraphs 32 and 34) and Fig. 8 #s 54 and 66**

1       3. A method of determining similarity between portions of gene  
2 expression profiles comprising the steps of:

3       processing data embodying a number of gene expression profiles  
4 with a similar sequences algorithm in a computer that is a time and  
5 intensity invariant correlation function to obtain a data set of  
6 gene expression pairs and a match fraction for each pair; **Page**  
7, **Line 31 - Page 8, Line 9 (Paragraph 36) and Fig. 1, # 213, 215**

8       choosing a threshold match fraction; **Page 13 Lines 6-20**  
9       **(Paragraph 52) sentence 6 and Fig. 2 # 217**

10       listing gene expression pairs in clusters by their match  
11 fractions above the threshold; **Page 13 Lines 15-20 (Paragraph 52)**  
12       **and Fig. 2 #s 221, 215, 219 and 223**

13       adding each gene not already in a cluster to a cluster having  
14 another gene having a highest match fraction with the each gene  
15 without regard of the threshold; **Page 9 Lines 8-14 (Paragraph 40)**  
16       **and Fig 2 # 229**

17       removing a first gene from a cluster when the first gene is  
18 also in another cluster which has another gene with a higher match  
19 fraction with the first gene than any of the genes in the cluster  
20 have with the first gene; **Page 8 Line 27-Page 9 Line 7 (Paragraph**  
21       **39) first sentence and Fig. 2 # 225**

22       repeating the removing step until all genes are listed in only  
23 one cluster; **Page 8 Line 27-Page 9 Line 7 (Paragraph 39) last**  
24       **sentence**

25       providing output of the listing of clusters of gene  
26 expression profiles. **Page 6 Lines 24-31 and Page 7 Lines 19-24**  
27       **(Paragraphs 32 and 34) and Fig. 8 #s 54 and 66**

1           4. A method for determining similarity between portions of gene  
2 expression profiles comprising the steps of:

3           processing a number of gene expression profiles with a similar  
4 sequences algorithm that is a time and intensity invariant  
5 correlation function with a computer to obtain a data set of gene  
6 expression pairs and a match fraction for each pair; **Page 7, Line 31-**  
7 **Page 8, Line 9 (Paragraph 36) and Fig. 1, # 213, 215**

8           choosing a threshold match fraction; **Page 13 Lines 5-20**  
9 **(Paragraph 52) sentence 6 and Fig. 2 # 217**

10           listing gene expression pairs in clusters by their match  
11 fractions above the threshold; **Page 8 Lines 16-26 (paragraph 38) and**  
12 **Fig. 2 # 223**

13           adding each gene not already in a cluster to a cluster having  
14 another gene having a highest match fraction disregarding the  
15 threshold with the each gene; **Page 9 Lines 8-14 (Paragraph 40) and**  
16 **Fig 2 # 229**

17           removing a first gene from a first cluster when the first gene  
18 is also in a second cluster which has another gene with a higher  
19 match fraction with the first gene than any of the genes in the  
20 first cluster have with the first gene, **Page 8 Line 27-Page 9 Line 7**  
21 **(Paragraph 39) first sentence and Fig. 2 # 225**

22           but;

23           retaining the first gene in the first cluster and removing the  
24 first gene from the second cluster when the difference between the  
25 highest match fraction of the first gene with a gene in the first  
26 cluster and the highest match fraction of the first gene with a gene  
27 in the second cluster is less than a minimum difference threshold  
28 and the number of subsequences represented in the similar gene pair  
29 having the highest match fraction in the first cluster is higher  
30 than the number of subsequences represented in the similar gene pair

1 having the highest match fraction in the second cluster; **Page 8 Line**  
2 **27-Page 9 Line 7 (Paragraph 39) second sentence and Fig. 2 # 225**

3

4 repeating the removing and retaining steps until all genes are  
5 listed in only one cluster; **Page 8 Line 27-Page 9 Line 7 (Paragraph**  
6 **39) last sentence**

7 providing output of the listing of clusters of gene  
8 expression profiles. **Page 6 Lines 24-31 and Page 7 Lines 19-24**  
9 **(Paragraphs 32 and 34) and Fig. 8 #s 54 and 66**

10

1       5. A method in a computer for determining similarity between  
2 genes comprising the steps of:

3           listing genes to be compared in a data set by their gene  
4 expression profiles; **Page 7,Line 31-Page 8,Line 9 (Paragraph 36)**  
5 **second sentence and Fig. 1 # 211**

6           processing the listed gene expression profiles with a similar  
7 sequences algorithm that is a time and intensity invariant  
8 correlation function to obtain a data set of gene expression pairs  
9 and a match fraction for each pair; **Page 7,Line 31-Page 8,Line 9**  
10 **(Paragraph 36) and Fig. 1, # 213, 215**

11           choosing a threshold match fraction; **Page 13 Lines 5-20**  
12 **(Paragraph 52) sentence 6 and Fig.2 # 217**

13  
14           creating a set G in which to list indices of genes accounted  
15 for; **Page 8 Lines 11-14 (Paragraph 37) and Fig. 2 # 217**

16           assigning genes i and j to a cluster a if they have a match  
17 fraction greater than the threshold; **Page 8 Lines 16-26 (Paragraph**  
18 **38) second sentence and Fig. 2 # 223 -> ca={i,j,...}**

19           assigning gene k to the cluster a if it has a match fraction  
20 greater than the threshold with either gene i or gene j;  
21 **Page 8 Lines 16-26 (Paragraph 38) last sentence and Fig. 2 # 223 ->**  
22 **ca={i,j,k,...}**

23           assigning genes k and l to a cluster b if they have a match  
24 fraction greater than the threshold and if both gene k and gene l do  
25 not have match fractions above the threshold with either gene i or  
26 gene j;

27 **Page 8 Lines 16-26 (Paragraph 38) and Fig. 2 # 223 -> cb={k,l,...}**  
28           repeating the assigning steps until all genes to be compared  
29 have been considered; **Page 13 Lines 5-20 (Paragraph 52) first two**  
30 **sentences and Fig #s 217, 219, and 229**

1 removing a first gene from a cluster when another cluster has  
2 another gene with a higher match fraction with the first gene; **Page**  
3 **8 Line 27-Page 9 Line 7 (Paragraph 39) second sentence and Fig. 2 #**  
4 **225**

5 repeating the removing step until all genes are listed in only  
6 one cluster; **Page 8 Line 27-Page 9 Line 7 (Paragraph 39) last**  
7 **sentence**

8 providing output of the listing of clusters of gene  
9 expression profiles. **Page 6 Lines 24-31 and Page 7 Lines 19-24**  
10 **(Paragraphs 32 and 34) and Fig. 8 #s 54 and 66**

11

12

1           6. A method in a computer for determining similarity between  
2 genes comprising the steps of:

3           listing genes to be compared in a data set by their gene  
4 expression profiles; **Page 7,Line 31-Page 8,Line 9 (Paragraph 36)**  
**second sentence and Fig. 1 # 211**

5           processing the listed gene expression profiles with a similar  
6 sequences algorithm that is a time and intensity invariant  
7 correlation function to obtain a data set of gene expression pairs  
8 and a match fraction for each pair; **Page 7,Line 31-Page 8,Line 9**  
**(Paragraph 36) and Fig. 1, # 213, 215**

9           choosing a threshold match fraction; **Page 13 Lines 5-20**  
10           **(Paragraph 52) sentence 6 and Fig.2 # 217**

11           creating a set G in which to list indices of genes accounted  
12 for; **Page 13 Lines 5-20 (Paragraph 52) 3rd and 4th sentences and**  
13 **Fig. 2 # 217**

14           assigning genes i and j to cluster 1 if they have a match  
15 fraction greater than the threshold; **Page 13 Line 21-Page 14 Line 6**  
16           **and Page 14 Lines 8-12 (Paragraphs 53 and 54) first sentence and**  
17 **Table IV**

18           assigning gene k to cluster 1 if it has a match fraction  
19 greater than the threshold with either gene i or gene j; **Page 13**  
20 **Line 21-Page 14 Line 6, Page 14 Lines 8-12, Page 14 Line 24-Page 15**  
21 **Line 3 (Paragraphs 53, 54 2nd sentence, 56) and Table IV**

22           assigning genes k and l to cluster 2 if they have a match  
23 fraction greater than the threshold and if both gene k and gene l do  
24 not have match fractions above the threshold with either gene i or  
25 gene j; **Page 13 Line 21-Page 14 Line 6, Page 14 Lines 8-12, Page 14**  
26 **Line 24-Page 15 Line 3 (Paragraphs 53, 54 2nd sentence, 56) and**  
27 **Table IV and Fig. 2 # 225**

28           removing a first gene from a cluster when another cluster has  
29 another gene with a higher match fraction with the first gene,

1 unless the another gene requires a larger number of subsequences to  
2 achieve similarity with the first gene; **Page 14 Line 24 - Page 15**  
3 **Line 3 (Paragraph 56) beginning at the 3rd sentence and Fig. 2 # 225**  
4 repeating the removing step until all genes are listed in only  
5 one cluster; **Page 8 Line 27-Page 9 Line 7 (Paragraph 39) last**  
6 **sentence**

7 providing output of the listing of clusters of gene  
8 expression profiles. **Page 6 Lines 24-31 and Page 7 Lines 19-24**  
9 **(Paragraphs 32 and 34) and Fig. 8 #s 54 and 66**

10  
11

1           10. A program product having computer readable code stored on a  
2 recordable media for determining similarity between portions of gene  
3 expression profiles comprising:

4           programmed means for processing a number of gene expression  
5 profiles with a similar sequences algorithm that is a time and  
6 intensity invariant correlation function to obtain a data set of  
7 gene expression pairs and a match fraction for each pair;

8 **Page 7,Line 31-Page 8,Line 9 (Paragraph 36) and Fig. 1, # 213, 215**

9           programmed means for listing gene expression pairs in clusters  
10 by their match fractions; **Page 8 Lines 16-26 (paragraph 38) and**  
11 **Fig.2 # 223**

12           programmed means for removing a first gene from a cluster when  
13 the first gene is also in another cluster which has another gene  
14 with a higher match fraction with the first gene than any of the  
15 genes in the cluster have with the first gene; **Page 8 Line 27-Page 9**  
16 **Line 7 (paragraph 39) and Fig. 2 # 225**

17           programmed means for repeating the removing step until all  
18 genes are listed in only one cluster. **Page 8 Line 27-Page 9 Line 7**  
19 **(Paragraph 39) last sentence**

1           11. A program product having computer readable code stored on a  
2 recordable media for determining similarity between portions of gene  
3 expression profiles using output from a similar sequences algorithm  
4 that is a time and intensity invariant correlation function  
5 comprising:

6           programmed means for providing a gene expression profile data  
7 set as input to programmed means embodying a similar sequences  
8 algorithm that is a time and intensity invariant correlation  
9 function to obtain a data set of gene expression pairs and a match  
10 fraction for each pair as output from the programmed means embodying  
11 a similar sequences algorithm; **Page 7, Line 31-Page 8, Line 9; Page**  
12 **10, Line 22-Page 11, Line 7 (Paragraphs 36, 44) and Fig. 1, # 213,**  
13 **215)**

14           programmed means for listing the gene expression pairs in  
15 clusters by their match fractions; **Page 7, Line 31-Page 8, Line 9**  
16 **(Paragraph 36) beginning at the second sentence and Fig. 1 # 215**

17  
18           programmed means for removing a first gene from a cluster when  
19 the first gene is also in another cluster which has another gene  
20 with a higher match fraction with the first gene than any of the  
21 genes in the cluster have with the first gene; **Page 8 Line 27-Page 9**  
22 **Line 7 (Paragraph 39) first sentence and Fig. 2 # 225**

23           programmed means for repeating the removing step until all  
24 genes are listed in only one cluster. **Page 8 Line 27-Page 9 Line 7**  
25 **(Paragraph 39) last sentence**

1           12. A program product having computer readable code stored on a  
2 recordable media for determining similarity between portions of gene  
3 expression profiles comprising the steps of:

4           programmed means for processing a number of gene expression  
5 profiles with a similar sequences algorithm that is a time and  
6 intensity invariant correlation function to obtain a data set of  
7 gene expression pairs and a match fraction for each pair; **Page**  
8 **7, Line 31-Page 8, Line 9 (Paragraph 36) and Fig. 1, # 213, 215**

9           programmed means for listing gene expression pairs in clusters  
10 by their match fractions; **Page 8 Lines 16-26 (paragraph 38) and**  
11 **Fig. 2 # 223**

12           programmed means for removing a first gene from a first cluster  
13 when the first gene is also in a second cluster which has another  
14 gene with a higher match fraction with the first gene than any of  
15 the genes in the first cluster have with the first gene, **Page 8 Line**  
16 **27-Page 9 Line 7 (Paragraph 39) first sentence and Fig. 2 # 225**  
17 but;

18           programmed means for retaining the first gene in the first  
19 cluster and removing the first gene from the second cluster when the  
20 difference between the highest match fraction of the first gene with  
21 a gene in the first cluster and the highest match fraction of the  
22 first gene with a gene in the second cluster is less than a minimum  
23 difference threshold and the number of subsequences represented in  
24 the similar gene pair having the highest match fraction in the first  
25 cluster is higher than the number of subsequences represented in the  
26 similar gene pair having the highest match fraction in the second  
27 cluster; **Page 8 Line 27-Page 9 Line 7 (Paragraph 39) second sentence**  
28 **and Fig. 2 # 225**

29           programmed means for repeating the removing step until all  
30 genes are listed in only one cluster. **Page 8 Line 27-Page 9 Line 7**  
31 **(Paragraph 39) last sentence**

1       13. A program product having computer readable code stored on a  
2 recordable media for determining similarity between portions of gene  
3 expression profiles comprising the steps of:

4       programmed means for processing a number of gene expression  
5 profiles with a similar sequences algorithm that is a time and  
6 intensity invariant correlation function to obtain a data set of  
7 gene expression pairs and a match fraction for each pair; **Page**  
8 **7, Line 31-Page 8, Line 9 (Paragraph 36) and Fig. 1, # 213, 215**

9       programmed means for choosing a threshold match fraction; **Page**  
10 **13 Lines 6-20 (Paragraph 52) sentence 6 and Fig.2 # 217**

11       programmed means for listing gene expression pairs in clusters  
12 by their match fractions above the threshold; **Page 8 Lines 16-26**  
13 **(paragraph 38) and Fig.2 # 223**

14       programmed means for adding each gene not already in a cluster  
15 to a cluster having another gene having a highest match fraction  
16 with the each gene without regard of the threshold; **Page 9 Lines 8-**  
17 **14 (Paragraph 40) and Fig 2 # 229**

18       programmed means for removing a first gene from a cluster when  
19 the first gene is also in another cluster which has another gene  
20 with a higher match fraction with the first gene than any of the  
21 genes in the cluster have with the first gene; **Page 8 Line 27-Page 9**  
22 **Line 7 (Paragraph 39) first sentence and Fig. 2 # 225**

23       programmed means for repeating the removing step until all  
24 genes are listed in only one cluster. **Page 8 Line 27-Page 9 Line 7**  
25 **(Paragraph 39) last sentence**

1           14. A program product having computer readable code stored on a  
2 recordable media for determining similarity between portions of gene  
3 expression profiles comprising the steps of:

4           programmed means for processing a number of gene expression  
5 profiles with a similar sequences algorithm that is a time and  
6 intensity invariant correlation function to obtain a data set of  
7 gene expression pairs and a match fraction for each pair; **Page**  
8 **7, Line 31-Page 8, Line 9 (Paragraph 36) and Fig. 1, # 213, 215**

9           programmed means for choosing a threshold match fraction; **Page**  
10 **13 Lines 6-20 (Paragraph 52) sentence 6 and Fig. 2 # 217**

11           programmed means for listing gene expression pairs in clusters  
12 by their match fractions above the threshold; **Page 8 Lines 16-26**  
13 **(paragraph 38) and Fig. 2 # 223**

14           programmed means for adding each gene not already in a cluster  
15 to a cluster having another gene having a highest match fraction  
16 disregarding the threshold with the each gene; **Page 9 Lines 8-14**  
17 **(Paragraph 40) and Fig 2 # 229**

18           programmed means for removing a first gene from a first cluster  
19 when the first gene is also in a second cluster which has another  
20 gene with a higher match fraction with the first gene than any of  
21 the genes in the first cluster have with the first gene, **Page 8 Line**  
22 **27-Page 9 Line 7 (Paragraph 39) first sentence and Fig. 2 # 225**  
23 but;

24           programmed means for retaining the first gene in the first  
25 cluster and removing the first gene from the second cluster when the  
26 difference between the highest match fraction of the first gene with  
27 a gene in the first cluster and the highest match fraction of the  
28 first gene with a gene in the second cluster is less than a minimum  
29 difference threshold and the number of subsequences represented in  
30 the similar gene pair having the highest match fraction in the first  
31 cluster is higher than the number of subsequences represented in the

1 similar gene pair having the highest match fraction in the second  
2 cluster; **Page 8 Line 27-Page 9 Line 7 (Paragraph 39) second sentence**  
3 **and Fig. 2 # 225**

4 programmed means for repeating the removing and retaining steps  
5 until all genes are listed in only one cluster. **Page 8 Line 27-Page**  
6 **9 Line 7 (Paragraph 39) last sentence**

1        15. A program product having computer readable code stored on a  
2 recordable media for determining similarity between genes comprising  
3 the steps of:

4        programmed means for listing genes to be compared by their gene  
5 expression profiles; **Page 7,Line 31-Page 8,Line 9 (Paragraph 36)**

6 **second sentence and Fig. 1 # 211**

7        programmed means for processing the listed gene expression  
8 profiles with a similar sequences algorithm that is a time and  
9 intensity invariant correlation function to obtain a data set of  
10 gene expression pairs and a match fraction for each pair; **Page**  
11 **7,Line 31-Page 8,Line 9 (Paragraph 36) and Fig. 1, # 213, 215**

12        programmed means for choosing a threshold match fraction; **Page**  
13 **13 Lines 6-20 (Paragraph 52) sentence 6 and Fig.2 # 217**

14        programmed means for creating a null set G(0) to hold genes  
15 accounted for; **Page 13 Lines 6-20 (Paragraph 52) 3rd and 4th**  
16 **sentences and Fig. 2 # 217**

17        programmed means for assigning genes i and j to cluster 1 if  
18 they have a match fraction greater than the threshold; **Page 13 Line**  
19 **21-Page 14 Line 6 and Page 14 Lines 8-12 (Paragraphs 53 and 54)**

20 **first sentence and Table IV**

21        programmed means for assigning gene k to cluster 1 if it has a  
22 match fraction greater than the threshold with either gene i or gene  
23 j; **Page 13 Line 21-Page 14 Line 6, Page 14 Lines 8-12, Page 14 Line**  
24 **24-Page 15 Line 3 (Paragraphs 53, 54 2nd sentence, 56) and Table IV**

25        programmed means for assigning genes k and l to cluster 2 if  
26 they have a match fraction greater than the threshold and if both  
27 gene k and gene l do not have match fractions above the threshold  
28 with either gene i or gene j; **Page 13 Line 21-Page 14 Line 6, Page**  
29 **14 Lines 8-12, Page 14 Line 24-Page 15 Line 3 (Paragraphs 53, 54 2nd**  
30 **sentence, 56) and Table IV and Fig. 2 # 225**

1       programmed means for removing a first gene from a cluster when  
2       another cluster has another gene with a higher match fraction with  
3       the first gene; **Page 14 Line 24 - Page 15 Line 3 (Paragraph 56)**  
4       **beginning at the 3rd sentence and Fig. 2 # 225**

5       programmed means for repeating the removing step until all  
6       genes are listed in only one cluster. **Page 8 Line 27-Page 9 Line 7**  
7       **(Paragraph 39) last sentence**

8

1       16. A program product having computer readable code stored on a  
2 recordable media for determining similarity between genes comprising  
3 the steps of:

4       programmed means for listing genes to be compared by their gene  
5 expression profiles; **Page 7,Line 31-Page 8,Line 9 (Paragraph 36)**  
6 **second sentence and Fig. 1 # 211**

7       programmed means for processing the listed gene expression  
8 profiles with a similar sequences algorithm that is a time and  
9 intensity invariant correlation function to obtain a data set of  
10 gene expression pairs and a match fraction for each pair; **Page**  
11 **7,Line 31-Page 8,Line 9 (Paragraph 36) and Fig. 1, # 213, 215**

12       programmed means for choosing a threshold match fraction; **Page**  
13 **13 Lines 5-20 (Paragraph 52) sentence 6 and Fig.2 # 217**

14       programmed means for creating a null set  $G(0)$  to hold genes  
15 accounted for; **Page 8 Lines 11-14 (Paragraph 37 and Fig. 2 # 217**

16       programmed means for assigning genes  $i$  and  $j$  to cluster 1 if  
17 they have a match fraction greater than the threshold; **Page 13 Line**  
18 **21-Page 14 Line 6 and Page 14 Lines 8-12 (Paragraphs 53 and 54)**  
19 **first sentence and Table IV**

20       programmed means for assigning gene  $k$  to cluster 1 if it has a  
21 match fraction greater than the threshold with either gene  $i$  or gene  
22  $j$ ; **Page 13 Line 21-Page 14 Line 6, Page 14 Lines 8-12, Page 14 Line**  
23 **24-Page 15 Line 3 (Paragraphs 53, 54 2nd sentence, 56) and Table IV**

24       programmed means for assigning genes  $k$  and  $l$  to cluster 2 if  
25 they have a match fraction greater than the threshold and if both  
26 gene  $k$  and gene  $l$  do not have match fractions above the threshold  
27 with either gene  $i$  or gene  $j$ ; **Page 13 Line 21-Page 14 Line 6, Page**  
28 **14 Lines 8-12, Page 14 Line 24-Page 15 Line 3 (Paragraphs 53, 54 2nd**  
29 **sentence, 56) and Table IV and Fig. 2 # 225**

1           programmed means for removing a first gene from a cluster when  
2   another cluster has another gene with a higher match fraction with  
3   the first gene, unless the another gene requires a larger number of  
4   subsequences to achieve similarity with the first gene; **Page 14 Line**  
5   **24 - Page 15 Line 3 (Paragraph 56) beginning at the 3rd sentence and**  
6   **Fig. 2 # 225**

7           programmed means for repeating the removing step until all  
8   genes are listed in only one cluster. **Page 8 Line 27-Page 9 Line 7**  
9   **(Paragraph 39) last sentence**

1           20. In a method of determining similarity between portions of  
2 gene expression profiles which includes processing a number of gene  
3 expression profiles using a computer with a similar sequences  
4 algorithm that is a time and intensity invariant correlation  
5 function to obtain a data set of gene expression pairs and a match  
6 fraction for each pair, **Page 7,Line 31-Page 8,Line 9 (Paragraph 36**  
7 **and Fig. 1, # 213, 215** the improvement comprising the steps of:

8           listing gene expression pairs in clusters by their match  
9 fractions; **Page 8 Lines 16-26 (paragraph 38) and Fig.2 # 223**

10           removing a first gene from a cluster when another cluster has  
11 another gene with a higher match fraction with the first gene,  
12 unless the another gene requires a larger number of subsequences to  
13 achieve similarity with the first gene; **Page 14 Line 24 - Page 15**  
14 **Line 3 (Paragraph 56) beginning at the 3rd sentence and Fig. 2 # 225**

15           repeating the removing step until all genes are listed in only  
16 one cluster; **Page 8 Line 27-Page 9 Line 7 (Paragraph 39) last**  
17 **sentence**

18           providing output of the listing of clusters of gene  
19 expression profiles. **Page 6 Lines 24-31 and Page 7 Lines 19-24**  
20 **(Paragraphs 32 and 34) and Fig. 8 #s 54 and 66**

21

22

23

24

(VI) Grounds of Rejection to be reviewed on Appeal

Claims 1-6, 10-16 and 20 are pending in this application.

Claims 7-9 and 17-19 were canceled after restriction.

The rejection of claims 1-6, 10-16 and 20 under 35 U.S.C. 101 is appealed.

The issues in this appeal are:

I. Whether claims 1, 2, 4, 6, 12, 14, 16 and 20 are indefinite under 35 U.S.C.112 second paragraph on the ground that the specification does not provide a meaning for the word "subsequences". The Examiner has found Figures 4 and 6 and paragraphs 48 - 50 to be unclear. It is believed that this issue has been resolved by applicants' remarks in the amendment after final.

II. Whether output to a user is a required claim step in order to define an invention, that is a practical application which is useful, concrete and tangible.

Claim 10 is representative of claims 1-6, 10-16 and 20 which have been rejected under 35 U.S.C. 101 and is related to Issue II.

III. Whether applicants' teaching of a personal computer with implicit, intrinsic and inherent output means in the specification support claims 1 - 6 and 20 as amended after final following the Examiners suggestion to recite "output . . . to a user" without adding new matter. The amendment after final was not entered on the ground that it added new matter.

1       Claim 1 is representative of claims 1 - 6, 20 which currently  
2       recite "providing output of the listing of clusters of gene  
3       expression profiles" and is related to Issues II and III.

4

5       Claims 1 - 6, 20 have been rejected when amended after final to  
6       recite "providing output of the listing of clusters of gene  
7       expression profiles **to a user**" as containing new matter

8

1                   (VII) Argument

2

3   Issue I   Whether claims 1, 2, 4, 6, 12, 14, 16 and 20 are  
4   indefinite under 35 U.S.C.112 second paragraph on the ground that  
5   the specification does not provide a meaning for the word  
6   "subsequences". The Examiner has found Figures 4 and 6 and  
7   paragraphs 48 – 50 to be unclear.

8

9   The specification at paragraph 15 recites:

10   [0015] According to the instant invention, two temporal sequences are similar and can be placed in  
11   the same cluster if they have enough non-overlapping time-ordered pairs of sub-sequences that are  
12   similar.

13   Paragraph 50 recites:

14   [0050] FIG. 4 exemplifies noise resistance and partial similarity. When one looks at *gene* 4 and *gene*  
15   3, it is clear that most likely, the value of 10 for *gene* 3 at t=3 is an outlier. This data point could have  
16   occurred, either from manual error or instrumentation error. The Agrawal Fast Similarity Search  
17   algorithm will minimize this artifact data point by its design, and identify two matching areas. The  
18   profile from t=1 to t=2 is identified as one subsequence and the profile from t=4 to t=6 as another  
19   subsequence. Since it has minimized this "outlier or noise", it is able to identify these two genes as  
20   similar in function.

21

22   Applicants believe that it is clear to those skilled in the art that  
23   the genes 3 and 4 in Figure 4 are temporal sequences from time 1  
24   through time 6 and that each sequence includes subsequences from  
25   time 1 to time 2 and from time 4 to time 6.

26

27   In view of the Examiners finding that the above remarks presented in  
28   the amendment after final were persuasive, it is believed that this  
29   issue has been resolved and would be removed if the amendment after  
30   final were entered.

1       **Issue II:** Whether output to a user is a required claim step in order  
2       to define an invention, that is a practical application which is  
3       useful, concrete and tangible.

4

5           Appellants claim in representative claim 10:

6           10. A program product having computer readable code stored on a  
7       recordable media for determining similarity between portions of gene  
8       expression profiles comprising:

9           programmed means for processing a number of gene expression  
10      profiles with a similar sequences algorithm that is a time and  
11      intensity invariant correlation function to obtain a data set of  
12      gene expression pairs and a match fraction for each pair; **Page**  
13      **7,Line 31-Page 8,Line 9 (Paragraph 36) and Fig. 1, # 213, 215**

14           programmed means for listing gene expression pairs in clusters  
15      by their match fractions; **Page 8 Lines 16-26 (paragraph 38) and**  
16      **Fig.2 # 223**

17           programmed means for removing a first gene from a cluster when  
18      the first gene is also in another cluster which has another gene  
19      with a higher match fraction with the first gene than any of the  
20      genes in the cluster have with the first gene; **Page 8 Line 27-Page 9**  
21      **Line 7 (paragraph 39) and Fig. 2 # 225**

22           programmed means for repeating the removing step until all  
23      genes are listed in only one cluster. **Page 8 Line 27-Page 9 Line 7**  
24      **(Paragraph 39) last sentence**

1       Applicants believe that the specification and claims indeed do  
2 describe a method and a program product that produce a result that  
3 has substantial and credible utility as required by MPEP 2107 II and  
4 that the claims are limited to a narrow practical application in a  
5 computer related art.

6  
7       The Examiner relies on the "New Interim Guidelines" to  
8 interpret the requirements of the Federal Courts under the current  
9 law to require claiming "output to a user". Applicants believe that  
10 the Examiner is mistaken and is applying an interpretation of the  
11 definition of the word tangible that is:

12      1) narrower than appropriate under the current law and is  
13      2) narrower than required under the "New Guidelines".

14  
15       1) The introduction to the "New Guidelines" states:  
16 "These Examination Guidelines ("Guidelines") are based on the USPTO's current understanding of  
17 the law and are believed to be fully consistent with binding precedent of the Supreme Court, the  
18 Federal Circuit and the Federal Circuit's predecessor courts. These Guidelines do not constitute  
19 substantive rulemaking and hence do not have the force and effect of law."

20  
21       In following the "Guidelines", the Examiner appears to require  
22 separate interpretations of the words useful, concrete and tangible.

23  
24       Applicants' attorney has found no basis in any of the Federal  
25 Circuit opinions using these words that imply that these terms are  
26 to have separate meanings. They appear to always be used together  
27 as synonyms for the concept of being useful and non-abstract.  
28 Applicants' attorney has requested that the Examiner provide a  
29 citation to a court's requirement that these terms are part of a  
30 three pronged test if such is the case in order to help applicants

1 decide whether to appeal or request continued examination. No  
2 citation was provided.

3 2) Even under the "Guidelines, the Examiners interpretation of  
4 the word tangible is unnecessarily narrow.

5 The "Guidelines" at page 13 recite

6 "Accordingly, a complete definition of the scope of 35 U.S.C. § 101, reflecting Congressional intent,  
7 is that any new and useful process, machine, manufacture or composition of matter under the sun that  
8 is made by man is the proper subject matter of a patent. The subject matter courts have found to be  
9 outside of, or exceptions to, the four statutory categories of invention is limited to abstract ideas, laws  
10 of nature and natural phenomena. While this is easily stated, determining whether an applicant is  
11 seeking to patent an abstract idea, a law of nature or a natural phenomenon has proven to be  
12 challenging."

13  
14 Beginning at page 21 the "Guidelines" recite:  
15

"TANGIBLE RESULT"

16 "The tangible requirement does not necessarily mean that a claim must either be tied to a particular  
17 machine or apparatus or must operate to change articles or materials to a different state or thing.  
18 However, the tangible requirement does require that the claim must recite more than a § 101 judicial  
19 exception, in that the process claim must set forth a practical application of that § 101 judicial exception  
20 to produce a real-world result. Benson, 409 U.S. at 71-72, 175 USPQ at 676-77 (invention ineligible  
21 because had "no substantial practical application."). "[A]n application of a law of nature or mathematical  
22 formula to a ... process may well be deserving of patent protection." Diehr, 450 U.S. at 187, 209 USPQ  
23 at 8 (emphasis added); see also Corning, 56 U.S. (15 How.) at 268, 14 L.Ed. 683 ("It is for the discovery  
24 or invention of some practical method or means of producing a beneficial result or effect, that a patent is  
25 granted . . .").

26  
27 In other words, the opposite meaning of "tangible" is "abstract."  
28 The bare conversion of any binary data as in Gottschalk V. Benson or  
29 the bubble sort of any data as in "Warmerdam, 33 F.3d at 1360, 31 USPQ2d at 1759  
30 ("steps of 'locating' a medial axis, and 'creating' a bubble hierarchy . . . describe nothing more than the

1 manipulation of basic mathematical constructs, the paradigmatic ‘abstract idea’”))” recited at  
2 page 14 of the “Guidelines” are examples of the abstract.

3

4 Applicants’ process does not convert or process just any data but is  
5 limited to useful concrete and non-abstract gene expression profiles  
6 in a data base of such profiles. Applicants’ process is but one  
7 application of many possible applications of the mathematical steps  
8 involved in obtaining the useful result.

9

10 At page 17 of the “Guidelines we see:

11 While abstract ideas, natural phenomena, and laws of nature are not eligible for patenting, methods and  
12 products employing abstract ideas, natural phenomena, and laws of nature to perform a real-world  
13 function may well be. In evaluating whether a claim meets the requirements of section 101, the claim  
14 must be considered as a whole to determine whether it is for a particular application of an abstract idea,  
15 natural phenomenon, or law of nature, rather than for the abstract idea, natural phenomenon, or law of  
16 nature itself.

17

18 As is clear from the specification and the claim limitations,  
19 applicants’ process is limited to a particular practical application  
20 and is not an abstract idea, natural phenomenon or a law of nature.

21

22 The result is that all of the processed gene expression profiles are  
23 each listed in only one cluster. This result of applicants’ claims  
24 is a very useful, repeatable and non-abstract result which is  
25 recognized by those skilled in the medical and computer arts to be  
26 of great value and useful, non-abstract and concrete finding of  
27 similar gene expression profiles.

28

1       **PRIOR ART**

2       Applicants note that their claims have not been rejected on prior  
3       art yet have been restricted on the ground that there were two  
4       groups of claims that required two fields of search. It is not  
5       apparent whether relevant prior art patents were considered by the  
6       Examiner while examining this application. It is believed that the  
7       "Guidelines" on page 10 are helpful in determining both the novelty  
8       of applicants' invention and the **usefulness and non-abstract nature**  
9       of applicants' the invention.

10  
11      As evidenced by the references which applicants have attempted to  
12      incorporate by reference, but have acquiesced to the Examiners  
13      correct requirement to cancel, in addition to applicants teachings  
14      in the background art section of their specification, users in the  
15      medical profession find great value and usefulness in methods for  
16      finding similar gene expression profiles that are tangible and  
17      concrete. See for example US Patent 6,406,853 abstract and claims  
18      25, 26 and US Patent 6,436,642 column 26 beginning at line 15.

19  
20      It is believed that if the rejections under 35 U.S.C. 101 put forth  
21      in this application were appropriate, many of the relevant prior art  
22      patents in the appropriate fields of search would be found to be  
23      invalid. Since they were issued under the guidance of current  
24      statutory law and court cases, it must be that the rejections in  
25      this application are based upon excessively narrow and untenable  
26      interpretation of the current law.

1           **Issue III:** Whether applicants' teaching of a personal computer  
2 with implicit, intrinsic and inherent output means in the  
3 specification support claims 1 - 6 as applicants have attempted to  
4 amended them after final without adding new matter.

5  
6           Appellants claim in representative claim 1:

7           1. A method for determining similarity between portions of gene  
8 expression profiles in a computer comprising the steps of:

9           processing a number of gene expression profiles with a similar  
10 sequences algorithm that is a time and intensity invariant  
11 correlation function to obtain a data set of gene expression profile  
12 pairs and a match fraction for each gene expression profile pair;

13 **Page 7, Line 31-Page 8, Line 9 (Paragraph 36) and Fig. 1, # 213, 215**

14           listing gene expression profile pairs in clusters by their  
15 match fractions; **Page 8 Lines 16-26 (paragraph 38) and Fig. 2 # 223**

16           removing a first gene expression profile from a cluster when  
17 another cluster has another gene expression profile with a higher  
18 match fraction with the first gene expression profile, unless the  
19 another gene expression profile requires a larger number of  
20 subsequences to achieve similarity with the first gene expression  
21 profile; **Page 8 Line 27-Page 9 Line 7 (paragraph 39) and Fig. 2 #**  
22 **225**

23           repeating the removing step until all gene expression profiles  
24 are listed in only one cluster; **Page 8 Line 27-Page 9 Line 7**  
25 **(Paragraph 39) last sentence**

26           providing output of the listing of clusters of gene  
27 expression profiles. **Page 6 Lines 24-31 and Page 7 Lines 19-24**  
28 **(Paragraphs 32 and 34) and Fig. 8 #s 54 and 66**

29

1        The Examiner has suggested that the claims must recite "output  
2 to a user", however the Examiner has stated that applicant's  
3 amendment after final of claim 1 to recite "providing output of the  
4 listing of clusters of gene expression profiles **to a user**" has added  
5 new matter.

6  
7        Applicants' specification recites: "[0030] The focal point of  
8 the preferred personal computer architecture comprises a processor  
9 51. The processor 51 is connected to a bus 52 which comprises a set  
10 of data lines, a set of address lines and a set of control lines. A  
11 plurality of I/O devices, memory and storage devices 53-58 and 66  
12 are connected to the bus 52 through separate adapters 59-64 and 67,  
13 respectively. For example, the display 54 may be either a CRT or a  
14 flat panel display."

15  
16        It is believed to be well known in the art as exemplified by  
17 prior art patents that users in the medical profession receive  
18 output from personal computer input/output devices such as  
19 applicants teach in their preferred embodiment. Again, applicants  
20 refer to US Patent 6,406,853 abstract and claims 25, 26 and US  
21 Patent 6,436,642 column 26 beginning at line 15.

22  
23        It is believed that material that is implicit, intrinsic, or  
24 inherent in the application as filed is not new matter.

25  
26        In order to be usable by a user, a personal computer  
27 necessarily and constantly exhibits the function of input and  
28 output, and such function was recognized as such by those skilled in  
29 the art of using personal computers. Therefore applicants' addition  
30 of the step of providing such output to satisfy the Examiner's  
31 reading of the guidelines was not new matter but is supported in

1       their specification by teachings that are implicit, intrinsic and  
2       inherent.

3  
4       Accordingly it is believed that the claims are clear, statutory  
5       and definite and are drawn to a novel and unobvious method and  
6       program product for clustering gene expression profiles which result  
7       is concrete, tangible and directly useful in drug selection and  
8       disease diagnosis.

9  
10       When applicants' amendment after final or an equivalent  
11       amendment is entered, the outstanding objection to the specification  
12       will be removed as applicants have therein canceled the attempted  
13       incorporation of US Patents 6,406,853 and 6,436,642 by reference.

14  
15  
16       **Request for Relief**

17  
18       Wherefore, Appellants respectfully request that the rejection  
19       of pending claims 1 - 6, 10 - 16 and 20 be reversed and in the  
20       alternative that applicants be allowed to amend the claims to recite  
21       "output to a user" without rejection for new matter.

22  
23       Respectfully submitted,

24  
25  
26  
27  
28         
29       Karl O. Hesse, Reg. No. 25,398  
30       Attorney for Appellants

31       Land line (704) 895-8241  
32       Cell phone (704) 724-1413  
33       Fax: (704) 594-8307

IBM Corporation  
Intellectual Property Law  
MG90-201/1  
8501 IBM Drive  
Charlotte, NC 28262-8563

1                   (VIII) Appendix

2                   Claims Involved in this Appeal

3

4                   1. A method for determining similarity between portions of gene  
5 expression profiles in a computer comprising the steps of:

6                   processing a number of gene expression profiles with a similar  
7 sequences algorithm that is a time and intensity invariant  
8 correlation function to obtain a data set of gene expression profile  
9 pairs and a match fraction for each gene expression profile pair;

10                  listing gene expression profile pairs in clusters by their  
11 match fractions;

12                  removing a first gene expression profile from a cluster when  
13 another cluster has another gene expression profile with a higher  
14 match fraction with the first gene expression profile, unless the  
15 another gene expression profile requires a larger number of  
16 subsequences to achieve similarity with the first gene expression  
17 profile;

18                  repeating the removing step until all gene expression profiles  
19 are listed in only one cluster;

20                  providing output of the listing of clusters of gene  
21 expression profiles.

1       2. A method for determining similarity between portions of gene  
2 expression profiles comprising the steps of:

3       processing a number of gene expression profiles with a similar  
4 sequences algorithm that is a time and intensity invariant  
5 correlation function to obtain a data set of gene expression pairs  
6 and a match fraction for each pair;

7       listing gene expression pairs in clusters by their match  
8 fractions;

9       removing a first gene from a first cluster when the first gene  
10 is also in a second cluster which has another gene with a higher  
11 match fraction with the first gene than any of the genes in the  
12 first cluster have with the first gene, but;

13       retaining the first gene in the first cluster and removing the  
14 first gene from the second cluster when the difference between the  
15 highest match fraction of the first gene with a gene in the first  
16 cluster and the highest match fraction of the first gene with a gene  
17 in the second cluster is less than a minimum difference threshold  
18 and the number of subsequences represented in the similar gene pair  
19 having the highest match fraction in the first cluster is higher  
20 than the number of subsequences represented in the similar gene pair  
21 having the highest match fraction in the second cluster;

22       repeating the removing step until all genes are listed in only  
23 one cluster;

24       providing output of the listing of clusters of gene  
25 expression profiles.

1       3. A method of determining similarity between portions of gene  
2 expression profiles comprising the steps of:

3       processing data embodying a number of gene expression profiles  
4 with a similar sequences algorithm in a computer that is a time and  
5 intensity invariant correlation function to obtain a data set of  
6 gene expression pairs and a match fraction for each pair;

7       choosing a threshold match fraction;

8       listing gene expression pairs in clusters by their match  
9 fractions above the threshold;

10      adding each gene not already in a cluster to a cluster having  
11 another gene having a highest match fraction with the each gene  
12 without regard of the threshold;

13      removing a first gene from a cluster when the first gene is  
14 also in another cluster which has another gene with a higher match  
15 fraction with the first gene than any of the genes in the cluster  
16 have with the first gene;

17      repeating the removing step until all genes are listed in only  
18 one cluster;

19      providing output of the listing of clusters of gene  
20 expression profiles.

1       4. A method for determining similarity between portions of gene  
2 expression profiles comprising the steps of:

3           processing a number of gene expression profiles with a similar  
4 sequences algorithm that is a time and intensity invariant  
5 correlation function with a computer to obtain a data set of gene  
6 expression pairs and a match fraction for each pair;

7           choosing a threshold match fraction;

8           listing gene expression pairs in clusters by their match  
9 fractions above the threshold;

10          adding each gene not already in a cluster to a cluster having  
11 another gene having a highest match fraction disregarding the  
12 threshold with the each gene;

13          removing a first gene from a first cluster when the first gene  
14 is also in a second cluster which has another gene with a higher  
15 match fraction with the first gene than any of the genes in the  
16 first cluster have with the first gene, but;

17          retaining the first gene in the first cluster and removing the  
18 first gene from the second cluster when the difference between the  
19 highest match fraction of the first gene with a gene in the first  
20 cluster and the highest match fraction of the first gene with a gene  
21 in the second cluster is less than a minimum difference threshold  
22 and the number of subsequences represented in the similar gene pair  
23 having the highest match fraction in the first cluster is higher  
24 than the number of subsequences represented in the similar gene pair  
25 having the highest match fraction in the second cluster;

26          repeating the removing and retaining steps until all genes are  
27 listed in only one cluster;

28          providing output of the listing of clusters of gene  
29 expression profiles.

1           5. A method in a computer for determining similarity between  
2 genes comprising the steps of:  
3           listing genes to be compared in a data set by their gene  
4 expression profiles;  
5           processing the listed gene expression profiles with a similar  
6 sequences algorithm that is a time and intensity invariant  
7 correlation function to obtain a data set of gene expression pairs  
8 and a match fraction for each pair;  
9           choosing a threshold match fraction;  
10          creating a set G in which to list indices of genes accounted  
11 for;  
12          assigning genes i and j to a cluster a if they have a match  
13 fraction greater than the threshold;  
14          assigning gene k to the cluster a if it has a match fraction  
15 greater than the threshold with either gene i or gene j;  
16          assigning genes k and l to a cluster b if they have a match  
17 fraction greater than the threshold and if both gene k and gene l do  
18 not have match fractions above the threshold with either gene i or  
19 gene j;  
20          repeating the assigning steps until all genes to be compared  
21 have been considered;  
22          removing a first gene from a cluster when another cluster has  
23 another gene with a higher match fraction with the first gene;  
24          repeating the removing step until all genes are listed in only  
25 one cluster;  
26          providing output of the listing of clusters of gene  
27 expression profiles.  
28

1       6. A method in a computer for determining similarity between  
2 genes comprising the steps of:  
3           listing genes to be compared in a data set by their gene  
4 expression profiles;  
5           processing the listed gene expression profiles with a similar  
6 sequences algorithm that is a time and intensity invariant  
7 correlation function to obtain a data set of gene expression pairs  
8 and a match fraction for each pair;  
9           choosing a threshold match fraction;  
10          creating a set G in which to list indices of genes accounted  
11 for;  
12          assigning genes i and j to cluster 1 if they have a match  
13 fraction greater than the threshold;  
14          assigning gene k to cluster 1 if it has a match fraction  
15 greater than the threshold with either gene i or gene j;  
16          assigning genes k and l to cluster 2 if they have a match  
17 fraction greater than the threshold and if both gene k and gene l do  
18 not have match fractions above the threshold with either gene i or  
19 gene j;  
20          removing a first gene from a cluster when another cluster has  
21 another gene with a higher match fraction with the first gene,  
22 unless the another gene requires a larger number of subsequences to  
23 achieve similarity with the first gene;  
24          repeating the removing step until all genes are listed in only  
25 one cluster;  
26          providing output of the listing of clusters of gene  
27 expression profiles.  
28

1           10. A program product having computer readable code stored on a  
2 recordable media for determining similarity between portions of gene  
3 expression profiles comprising:

4           programmed means for processing a number of gene expression  
5 profiles with a similar sequences algorithm that is a time and  
6 intensity invariant correlation function to obtain a data set of  
7 gene expression pairs and a match fraction for each pair;

8           programmed means for listing gene expression pairs in clusters  
9 by their match fractions;

10          programmed means for removing a first gene from a cluster when  
11 the first gene is also in another cluster which has another gene  
12 with a higher match fraction with the first gene than any of the  
13 genes in the cluster have with the first gene;

14          programmed means for repeating the removing step until all  
15 genes are listed in only one cluster.

1       11. A program product having computer readable code stored on a  
2 recordable media for determining similarity between portions of gene  
3 expression profiles using output from a similar sequences algorithm  
4 that is a time and intensity invariant correlation function  
5 comprising:

6       programmed means for providing a gene expression profile data  
7 set as input to programmed means embodying a similar sequences  
8 algorithm that is a time and intensity invariant correlation  
9 function to obtain a data set of gene expression pairs and a match  
10 fraction for each pair as output from the programmed means embodying  
11 a similar sequences algorithm;

12       programmed means for listing the gene expression pairs in  
13 clusters by their match fractions;

14       programmed means for removing a first gene from a cluster when  
15 the first gene is also in another cluster which has another gene  
16 with a higher match fraction with the first gene than any of the  
17 genes in the cluster have with the first gene;

18       programmed means for repeating the removing step until all  
19 genes are listed in only one cluster.

1           12. A program product having computer readable code stored on a  
2 recordable media for determining similarity between portions of gene  
3 expression profiles comprising the steps of:

4           programmed means for processing a number of gene expression  
5 profiles with a similar sequences algorithm that is a time and  
6 intensity invariant correlation function to obtain a data set of  
7 gene expression pairs and a match fraction for each pair;

8           programmed means for listing gene expression pairs in clusters  
9 by their match fractions;

10          programmed means for removing a first gene from a first cluster  
11 when the first gene is also in a second cluster which has another  
12 gene with a higher match fraction with the first gene than any of  
13 the genes in the first cluster have with the first gene, but;

14          programmed means for retaining the first gene in the first  
15 cluster and removing the first gene from the second cluster when the  
16 difference between the highest match fraction of the first gene with  
17 a gene in the first cluster and the highest match fraction of the  
18 first gene with a gene in the second cluster is less than a minimum  
19 difference threshold and the number of subsequences represented in  
20 the similar gene pair having the highest match fraction in the first  
21 cluster is higher than the number of subsequences represented in the  
22 similar gene pair having the highest match fraction in the second  
23 cluster;

24          programmed means for repeating the removing step until all  
25 genes are listed in only one cluster.

1       13. A program product having computer readable code stored on a  
2 recordable media for determining similarity between portions of gene  
3 expression profiles comprising the steps of:

4       programmed means for processing a number of gene expression  
5 profiles with a similar sequences algorithm that is a time and  
6 intensity invariant correlation function to obtain a data set of  
7 gene expression pairs and a match fraction for each pair;

8       programmed means for choosing a threshold match fraction;

9       programmed means for listing gene expression pairs in clusters  
10 by their match fractions above the threshold;

11       programmed means for adding each gene not already in a cluster  
12 to a cluster having another gene having a highest match fraction  
13 with the each gene without regard of the threshold;

14       programmed means for removing a first gene from a cluster when  
15 the first gene is also in another cluster which has another gene  
16 with a higher match fraction with the first gene than any of the  
17 genes in the cluster have with the first gene;

18       programmed means for repeating the removing step until all  
19 genes are listed in only one cluster.

1        14. A program product having computer readable code stored on a  
2 recordable media for determining similarity between portions of gene  
3 expression profiles comprising the steps of:

4            programmed means for processing a number of gene expression  
5 profiles with a similar sequences algorithm that is a time and  
6 intensity invariant correlation function to obtain a data set of  
7 gene expression pairs and a match fraction for each pair;

8            programmed means for choosing a threshold match fraction;

9            programmed means for listing gene expression pairs in clusters  
10 by their match fractions above the threshold;

11            programmed means for adding each gene not already in a cluster  
12 to a cluster having another gene having a highest match fraction  
13 disregarding the threshold with the each gene;

14            programmed means for removing a first gene from a first cluster  
15 when the first gene is also in a second cluster which has another  
16 gene with a higher match fraction with the first gene than any of  
17 the genes in the first cluster have with the first gene, but;

18            programmed means for retaining the first gene in the first  
19 cluster and removing the first gene from the second cluster when the  
20 difference between the highest match fraction of the first gene with  
21 a gene in the first cluster and the highest match fraction of the  
22 first gene with a gene in the second cluster is less than a minimum  
23 difference threshold and the number of subsequences represented in  
24 the similar gene pair having the highest match fraction in the first  
25 cluster is higher than the number of subsequences represented in the  
26 similar gene pair having the highest match fraction in the second  
27 cluster;

28            programmed means for repeating the removing and retaining steps  
29 until all genes are listed in only one cluster.

1       15. A program product having computer readable code stored on a  
2 recordable media for determining similarity between genes comprising  
3 the steps of:

4       programmed means for listing genes to be compared by their gene  
5 expression profiles;

6       programmed means for processing the listed gene expression  
7 profiles with a similar sequences algorithm that is a time and  
8 intensity invariant correlation function to obtain a data set of  
9 gene expression pairs and a match fraction for each pair;

10      programmed means for choosing a threshold match fraction;

11      programmed means for creating a null set G(0) to hold genes  
12 accounted for;

13      programmed means for assigning genes i and j to cluster 1 if  
14 they have a match fraction greater than the threshold;

15      programmed means for assigning gene k to cluster 1 if it has a  
16 match fraction greater than the threshold with either gene i or gene  
17 j;

18      programmed means for assigning genes k and l to cluster 2 if  
19 they have a match fraction greater than the threshold and if both  
20 gene k and gene l do not have match fractions above the threshold  
21 with either gene i or gene j;

22      programmed means for removing a first gene from a cluster when  
23 another cluster has another gene with a higher match fraction with  
24 the first gene;

25      programmed means for repeating the removing step until all  
26 genes are listed in only one cluster.

27

1       16. A program product having computer readable code stored on a  
2 recordable media for determining similarity between genes comprising  
3 the steps of:

4           programmed means for listing genes to be compared by their gene  
5 expression profiles;

6           programmed means for processing the listed gene expression  
7 profiles with a similar sequences algorithm that is a time and  
8 intensity invariant correlation function to obtain a data set of  
9 gene expression pairs and a match fraction for each pair;

10          programmed means for choosing a threshold match fraction;

11          programmed means for creating a null set G(0) to hold genes  
12 accounted for;

13          programmed means for assigning genes i and j to cluster 1 if  
14 they have a match fraction greater than the threshold;

15          programmed means for assigning gene k to cluster 1 if it has a  
16 match fraction greater than the threshold with either gene i or gene  
17 j;

18          programmed means for assigning genes k and l to cluster 2 if  
19 they have a match fraction greater than the threshold and if both  
20 gene k and gene l do not have match fractions above the threshold  
21 with either gene i or gene j;

22          programmed means for removing a first gene from a cluster when  
23 another cluster has another gene with a higher match fraction with  
24 the first gene, unless the another gene requires a larger number of  
25 subsequences to achieve similarity with the first gene;

26          programmed means for repeating the removing step until all  
27 genes are listed in only one cluster.

28

1       20. In a method of determining similarity between portions of  
2 gene expression profiles which includes processing a number of gene  
3 expression profiles using a computer with a similar sequences  
4 algorithm that is a time and intensity invariant correlation  
5 function to obtain a data set of gene expression pairs and a match  
6 fraction for each pair, the improvement comprising the steps of:

7       listing gene expression pairs in clusters by their match  
8 fractions;

9       removing a first gene from a cluster when another cluster has  
10 another gene with a higher match fraction with the first gene,  
11 unless the another gene requires a larger number of subsequences to  
12 achieve similarity with the first gene;

13       repeating the removing step until all genes are listed in only  
14 one cluster;

15       providing output of the listing of clusters of gene  
16 expression profiles.

17

#### (IX) Evidence Appendix

No evidence is being submitted in this appeal.

3

1                   **(X) Related Proceedings Appendix**

2                   None.